Bronchoalveolar lavage cytokines are of minor value to diagnose complications following lung transplantation

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Abstract: Early diagnosis and treatment of acute cellular rejection (ACR) may improve long-term outcome for lung transplant recipients (LTRs). Cytokines have become valuable diagnostic tools in many medical fields. The role of bronchoalveolar lavage (BAL) cytokines is of unknown value to diagnose ACR and distinguish rejection from infection. We hypothesized that distinct cytokine patterns obtained by surveillance bronchoscopies during the first year after transplantation are associated with ACR and microbiologic findings. We retrospectively analyzed data from 319 patients undergoing lung transplantation at University Hospital Zurich from 1998 to 2016. We compared levels of IL-6, IL-8, IFN- and TNF- in 747 BAL samples with transbronchial biopsies (TBB) and microbiologic results from surveillance bronchoscopies. We aimed to define reference values that would allow distinction between four specific groups "ACR", "infection", "combined ACR and infection" and "no pathologic process". No definitive pattern was identified. Given the overlap between groups, these four cytokines are not suitable diagnostic markers for ACR or infection after lung transplantation.

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Tables

Table 1

Patient characteristics.

Demographics	
Patients, n	319
Female, n (%)	142 (44.5%)
Male, n (%)	177 (55.5%)
Age at transplantation, mean ± standard deviation (range), year	51.8 ±15.5 (18-77)
CMV high-risk, n (%)	134 (42.1%)
Transplant indication	
COPD, n (%)	100 (31.3%)
Cystic fibrosis, n (%)	107 (33.5%)
Pulmonary fibrosis, n (%)	93 (29.1%)
Pulmonary hypertension, n (%)	17 (5.3%)
Re-Transplantation, n (%)	2 (0.6%)

Table 2

BAL cytokine concentrations for different specific groups. The concentrations [pg/ml] in the given group at the time of grade ≥ A1 ACR (R); viral, bacterial or fungal infection (I); “no pathologic process” (None) or “combined ACR and infection” (R+I) is shown as median and interquartile range (IQR). Significance for differences between categories was determined using Kruskal-Wallis test.

	Group	**Median [pg/ml]**	**IQR [pg/ml]**	**p-value**
IL-6	None	2.20	1.00 - 5.50	p = 0.045
	R	1.60	1.17 - 5.93	
	I	2.50	0.90 - 5.45	
	R+I	4.10	1.40 - 7.10	
IL-8	None	475.00	212.00 - 891.00	p = 0.7
	R	453.00	225.00 - 829.00	
	I	476.00	220.00 - 1151.50	
	R+I	585.00	255.00 - 1115.00	
TNF-α	None	0.11	0.01 - 0.30	p = 0.2
	R	0.10	0.00 - 0.45	
	I	0.20	0.03 - 0.50	
	R+I	0.10	0.00 - 0.68	
IFN-γ	None	0.10	0.00 - 1.20	p = 0.1
	R	0.10	0.00 - 0.20	
	I	0.10	0.00 - 1.02	
	R+I	0.10	0.010- 1.00	